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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/746,635	11/13/1996	VADIRAJA MURTHY	96700/341	7843

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/746,635	MURTHY ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2001 and 05 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Amendment Entry

1. Applicant's response filed 7/26/01 in Paper No. 38 and Supplemental amendment filed 9/5/01 in Paper No. 40 are acknowledged and have been entered. Claims 24-26 have been added. Claims 20 and 24-26 are pending and are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim 20 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)).

Olsson et al. found that 1) adenylate kinase was concomitantly released with hemoglobin during cell aging, 2) cell aging results in progressive lysis of erythrocytes, 3) adenylate kinase was suitable for monitoring hemolysis due to its extreme storage stability, 4) there was a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase, 5) and while hemolysis was conventionally measured by measuring extracellular hemoglobin, adenylate kinase activity measurement was also a sensitive and convenient way to follow hemolysis (see page 437, Table 1, and page 445). Olsson et al. determined adenylate kinase activity in plasma by measuring formation of ATP from ADP by firefly luciferase reaction.

Olsson et al. differ from the instant invention in failing to detect hemolysis by determining adenylate kinase activity in serum rather than plasma. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Olsson et al. by determining erythrocyte kinase activity in serum rather than plasma because serum and plasma are conventional alternative samples used in clinical analysis, differing only in the presence or absence of anticoagulation.

3. Claims 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)) as applied to claim 20 above, and further in view of Matsura et al. (Journal of Biological Chemistry, 264 (17): 10148-10155 (1989)).

Olsson et al. has been discussed supra. Olsson et al. differ from the instant invention in failing to teach determining adenylate kinase activity using an antibody specific for adenylate kinase.

Matsura et al. teach that there is an association between adenylate kinase activity (deficiency) in erythrocytes and hemolysis (hemolytic anemia) (see Abstract). Matsura et al. teach that adenylate kinase (AK1) is present in skeletal muscle, brain, and erythrocyte; thus, adenylate kinase activity has been totally and differentially measured (see page 10148, column 2). Specifically, Matsura et al. describe immunoblot analysis of human erythrocyte adenylate kinase using antibody (anti AK1 antibody) specific for adenylate kinase (see 10151).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to measure erythrocyte adenylate kinase activity in the method of Olsson using antibody specific for adenylate kinase such as taught by Matsura because use of antibody in determining the concentration of proteins, antigens, or in this case enzyme, is well known, conventional, and well within ordinary skill.

Response to Arguments

4. Applicant's arguments have been fully considered but they are not persuasive.

A) Applicant argues that Olsson never establishes a correlation between hemolysis and erythrocyte adenylate kinase.

Contrary to Applicant's contention, Olsson specifically teach that adenylate kinase is released concomitantly with hemoglobin (released from erythrocytes into

serum as a result of hemolysis) and that there is a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase; thus making adenylate kinase activity a suitable enzyme for measuring and monitoring hemolysis (see Abstract and page 437). While the instant invention is drawn to determining adenylate kinase activity as effected by in vivo or in situ hemolysis in patients due to physiologic or pathologic causes, Olsson's study is drawn to detecting adenylate kinase activity in stored blood cells as effected by leakage of adenylate kinase from aging of erythrocytes. A person with ordinary skill in the art at the time would have, however, appreciated the correlation between hemolysis and erythrocyte adenylate kinase suggested by Olsson as emphasized by the parallel between hemoglobin (a known indicator of hemolysis) and erythrocyte adenylate kinase.

In as far as Applicant's contention that in Olsson's study of adenylate kinase wherein two samples are from red blood cell population and one sample is from a whole blood sample, a significant amount of the adenylate kinase from the latter whole blood sample "could have been from platelets and not erythrocytes", it has been made clear by Olsson that for two of the three samples, adenylate kinase is from erythrocytes. Additionally, Applicant's statement that "adenylate kinase *could have been from* platelets" is an assertion without evidence; and thus, is given no merit.

5. Applicant's arguments have been considered but are not deemed persuasive. No claims are allowed.

6. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
8/21/03

Gailene R. Gabel
Art 1641
August 19, 2003